Dissecting early regulatory relationships in the lamprey neural crest gene network.

Journal: Proc Natl Acad Sci U S A

Publication Year: 2008

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PubMed link: 19104059

Funding Grants: Training in Stem Cell Biology at CIT

Public Summary:
This work examines the gene interactions that establish the border region between the forming central nervous system and presumptive epidermis. This region, called the neural plate border, contains cells that will give rise to the neural crest, an important vertebrate-specific cell population. By using the lamprey embryo, which develops very slowly, we are able to order the events that take place in this neural plate border and find that a factor called AP-2 is very important for starting off the process of neural plate border formation.

Scientific Abstract:
The neural crest, a multipotent embryonic cell type, originates at the border between neural and nonneural ectoderm. After neural tube closure, these cells undergo an epithelial-mesenchymal transition, migrate to precise, often distant locations, and differentiate into diverse derivatives. Analyses of expression and function of signaling and transcription factors in higher vertebrates has led to the proposal that a neural crest gene regulatory network (NC-GRN) orchestrates neural crest formation. Here, we interrogate the NC-GRN in the lamprey, taking advantage of its slow development and basal phylogenetic position to resolve early inductive events, 1 regulatory step at the time. To establish regulatory relationships at the neural plate border, we assess relative expression of 6 neural crest network genes and effects of individually perturbing each on the remaining 5. The results refine an upstream portion of the NC-GRN and reveal unexpected order and linkages therein; e.g., lamprey AP-2 appears to function early as a neural plate border rather than a neural crest specifier and in a pathway linked to MsxA but independent of ZicA. These findings provide an ancestral framework for performing comparative tests in higher vertebrates in which network linkages may be more difficult to resolve because of their rapid development.